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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,266	ONG ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1-3, 6 and 26-28 have been amended as requested in the amendment filed on June 4, 2008. Following the amendment, claims 1-3, 6 and 26-28 are pending and are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on June 4, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Rejections/Objections – Including New Grounds, Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. As currently amended, Claims 1-3, 6 and 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 1 and 26-28 are vague and indefinite in their recitation of administration "wherein said administration is carried out under conditions effective to ...". One of ordinary skill in the art would not be reasonably apprised as to the scope of those

required conditions and neither the claims themselves nor the specification explicitly define the requisite conditions.

6. The independent claim, Claim 1, is drawn to a method of treatment or prophylaxis of atherosclerosis. Dependent claims 2 and 3 are drawn to the method of claim 1 comprising "preventing the development of atherosclerotic plaques" or "treating pre-existing atherosclerosis". One of ordinary skill in the art would not be reasonably apprised as to how the scope of claims 2 and 3 differ from the parent claim. The claims do not recite further active steps which modify the method, such as assaying for a reduction in atherosclerosis or assaying for a decrease in atherosclerotic development and, thus, merely recite inherent results of carrying out said administration for prophylaxis. See also section 12 below.

7. Claim 6 is indefinite for depending from an indefinite claims.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-28 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record in the Office Action mailed December 4, 2007.

On pages 5-6 of Remarks filed June 4, 2008 Applicant traverses the rejection on the grounds that the specification identifies by incorporation by reference (page 9, lines

5-23) the members of the GHRP family and its derivatives and peptidomimetics (page 8, line 27 to page 9, line 5) that are encompassed by the "GHRP derivative, a derived peptidomimetic or a CD36 ligand" of the claims. Applicants conclude that one of ordinary skill would be fully aware of the various compounds that can be used in the method by "using known compounds within the recited classes". While this has been fully considered it is not found persuasive for the following reasons.

To reiterate, the claims are drawn to a genus of molecules (a growth hormone releasing peptide of Hexarelin family (GHRP), aGHRP derivative, a derived peptidomimetic or a CD36 ligand) that is defined by function ("which modulates the expression of a scavenger receptor B (CD36)" claim 27; "which modulates the expression of the ATP-binding cassette ABCA1 transporter and scavenger receptor B (CD36)" claim 28) and the instant specification fails to describe the entire genus of molecules that are encompassed by these claims.

Applicant is reminded that the requirement for written description under the first paragraph of section 112 is separate and distinct from the enablement requirement of that paragraph. See *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1116-17 (Fed. Cir. 1991). Compliance with the written description requirement is a question of fact. *Id.*

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. EliLilly and Co.*, 119 F.3d 1559, 1568,

43 USPQ2d 1398, 1405 (Fed. Cir. 1997 (bracketed material in original). The claims in *Lilly* were directed generically to vertebrate or mammalian insulin cDNAs. See id. at 1567, 43 USPQ2d at 1405. The court held that a structural description of a rat cDNA was not an adequate description of these broader classes of cDNAs.

The *Lilly* court explained that

> a generic statement such as... 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. at 1568, 43 USPQ2d at 1406. Finally, the *Lilly* court set out exemplary ways in which a genus of cDNAs could be described:

> A description of a genus of cDNAs may be achieved by means
>
> of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id. at 1569.

In *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002) the appellate court held that a claimed DNA could be described without, necessarily, disclosing its structure. The court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics.., i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or

some combination of such characteristics.'" *See id.* at 1324, 63 USPQ2d at 1613 (emphasis omitted, ellipsis and bracketed material in original).

The court has also noted that "*Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

It should be noted that this standard applies to peptides, such as in the instant claims, as well as DNAs. *See University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 925, 69 USPQ2d 1886, "893 (Fed. Cir. 2004): "We agree with Rochester that *Fiefs, Lilly,* and *Enzo* differ from this case in that they all related to genetic material whereas this case does not, but we find that distinction to be unhelpful to Rochester's position. It is irrelevant; the statute applies to all types of inventions. We see no reason for the rule to be any different when non-genetic materials are at issue."

In *University of Rochester*, the court held that the disclosure of general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of *which* peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims failed to meet the description requirement of § 112. *Id.* at 927, 69 USPQ2d at 1895. ("As pointed out by the district court, the '850 patent does not disclose just 'which "peptides, polynucleotides, and small organic

molecules" have the desired characteristic of selectively inhibiting PGHS-2.'... Without such disclosure, the claimed methods cannot be said to have been described.").

The Examiner has found that the instant disclosure as filed does not provide adequate written description to support the genus of molecules encompassed within the genus claimed, namely a growth hormone releasing peptide of Hexarelin family (GHRP), a GHRP derivative, a derived peptidomimetic or a CD36 ligand, and have failed to indicate a structure-to-function correlate for the peptides within the claimed genus that are capable of modulating the expression of a scavenger receptor B (CD36) or modulating the expression of both the ATP-binding cassette ABCA1 transporter and CD36, and the rejection is affirmed.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-3, 6 and 26-28 stand rejected under 35 U.S.C. 102(a) as being anticipated by Broglio et al. European Journal of Pharmacology, 448:193-200, May 10, 2002, for reasons of record in the previous Office Action.

On pages 6 and 7 of Remarks filed June 4, 2008, Applicant traverses the rejection on the grounds that while Broglio discusses an acute dose of hexarelin

administered to a patient who has coronary artery disease during by-pass surgery and reports improved cardiac function, Broglio does not report treatment or prevention of atherosclerosis. Applicant further argues that "the single dose of hexarelin described by Broglio would not necessarily achieve effective results (i.e. an effective treatment of pre-existing atherosclerosis or a prophylaxis thereof). The present application provides evidence that repeated daily dosage, on the other hand, is effective" (page 6, last 2 sentences). Applicant also states that "the same process remains patentable where the purpose of the process is different" and states that the purpose of the Broglio method was not for the treatment or prevention of atherosclerosis. These arguments have been fully considered but are not found persuasive for the following reasons.

The invention is drawn to a method of treatment or prophylaxis of atherosclerosis comprising the sole active step of administering one or more growth hormone releasing peptides (GHRPs) to a patient in need and dependent claims recite, wherein the one or more GHRPs are hexarelin or EP80317.

The Broglio prior art teaches a method comprising administering hexarelin administration to a patient with coronary artery disease receiving by-pass surgery. The instant disclosure identifies patients with coronary artery disease as encompassed by the invention (page 5). The Broglio reference specifically discloses that the patient had a history of prior myocardial infarction and evidence of atherosclerotic plaques as determined by angiography, thereby identifying the patient as one in need as defined by the instant disclosure (see Claim 3).

While Applicant suggests that the purpose of the administration is different, the claims merely recite the mere administration or "carrying out said administration" to a patient in need as sufficient to practice the method of treatment or prophylaxis of atherosclerosis. There is no requirement within the claims for a determination of a requisite degree of treatment or prophylaxis, such as "thereby reducing plaque accumulation by 50%", nor is there a limitation providing for "repeated daily dosages" as a requirement for effectiveness, as argued by Applicant in Remarks. Therefore, the instant method of the claims fails to distinguish over that of the prior art, and the method of Broglio fully anticipates the instantly claimed method.

11. Claims 1, 2, 6 and 26-28 stand as rejected under 35 U.S.C. 102(b) as being anticipated by Imbimbo (1994), as evidenced by the American Heart Association (AHA), Heart and Stroke Statistics—2002 Update, for reasons of record in the previous Office Action.

On pages 7-9 of Remarks filed June 4, 2008, Applicant traverses the rejection on the following grounds. Applicant states that while Imbimbo teaches "hexarelin administration to healthy male subjects", and the AHA 2002 report is "evidence that 90% of the (American) population has at least one risk factor for cardiovascular disease", "there is no suggestion or disclosure that the at least one risk factor would inevitably lead to atherosclerosis" (page 8, paragraphs 1 and 2). Applicant argues that the subjects of the Imbimbo study were not treated prophylactically because "it cannot be said that any subject of Imbimbo necessarily possessed at least one risk factor for

atherosclerosis" (*Id.*, paragraph 4). This argument has been considered in full but is not found persuasive for the following reasons.

The instant specification identifies the method as being performed in a patient at risk of developing a "plaque, hypercholesterolemia or cardiovascular disease" (page 5). The AHA 2002 report was relied upon as evidence that 90% of the general population have at least one risk factor for cardiovascular disease. Therefore, one of ordinary skill in the art would recognize that the instant method fails to distinguish over the method of Imbimbo, in which hexarelin was administered to male subjects from the general population. The instant claims read upon a method of prophylaxis of atherosclerosis comprising the sole active step of administration of hexarelin, wherein said administration is carried out under conditions effective to prevent atherosclerosis. Neither the claims themselves nor the specification define of those "conditions" essential for prevention. Nor is there a limitation with respect to limiting the subjects for whom administration would be effective for prophylaxis. Absent said recitation the method reads upon administration to 90% of the general population. Therefore, the rejection is maintained.

Double Patenting

12. Applicant is advised that should claim 1 be found allowable, claims 2 and 3 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing

one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

13. No Claim is allowed.

14. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M,W and ALT F 7 am to 3:30, T & R 5:30 -5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
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